

## Bulk Drug Substance to be Used in Pharmacy Compounding

Docket No. 98N-0182

### Bulk Drug Substance

Ingredient Name: Sodium Butyrate  
Chemical Name: Butyric acid, sodium salt CAS 156-54-7  
Chemical Grade or Strength: Minimum 98%  
How Supplied: White powder  
International Pharmacopeial Recognition: Unknown.  
Bibliography: 1) MSDS attached  
2) Medline search bibliography attached

### Compounded Product

Formulations: Short Chain Fatty Acid Enema. Aqueous solution for use as an enema.  
Enema Formulation: Sodium acetate 8.166 g  
Sodium propionate 2.882 g  
Sodium butyrate 4.404 g  
Sodium chloride 2.5 g  
Sterile water for irrigation qs 1000 mL

Strength(s): See above.  
Route of Administration: Rectally 60 mL as an enema.  
Past/Proposed Use: Treatment of colitis. No commercial formulation is available.  
Stability Data: None  
Additional Information: None

Nominated by: University of Texas M. D. Anderson Cancer Center  
Division of Pharmacy (Box 90)  
1515 Holcombe Blvd.  
Houston, Texas 77030

tel: (713) 792-2870



Database: Medline &lt;1966 to present&gt;

Set	Search	Results
1	fatty acid enemas.tw.	8
2	short chain fatty acid enemas.tw.	7
3	1 or 2	8

&lt;1&gt;

Unique Identifier

98089837

Authors

Sandborn WJ.

Title

Are short-chain fatty acid enemas effective for left-sided ulcerative colitis?.

Source

Gastroenterology. 114(1):218-9, 1998 Jan.

&lt;2&gt;

Unique Identifier

97211658

Authors

Cummings JH.

Institution

Addenbrooke's Hospital, MRC Dunn Clinical Nutrition Centre, Cambridge, UK.

Title

Short-chain fatty acid enemas in the treatment of distal ulcerative colitis [comment]. [Review] [27 refs]

Comments

Comment on: Eur J Gastroenterol Hepatol 1997 Feb;9(2):163-8

Source

European Journal of Gastroenterology &amp; Hepatology. 9(2):149-53, 1997 Feb.

&lt;3&gt;

Unique Identifier

97099404

Authors

Scheppach W.

Institution

Department of Medicine, University of Wurzburg, Germany.

Title

Treatment of distal ulcerative colitis with short-chain fatty acid enemas. A placebo-controlled trial.  
German-Austrian SCFA Study Group.

Digestive Diseases & Sciences. 41(11):2254-9. 1996 Nov.  
Abstract

Rectal enemas containing a short-chain fatty acid mixture, butyrate alone, or saline placebo were administered to 47 patients with active distal ulcerative colitis. Enemas were instilled twice daily and the patients' condition was evaluated at entry and after four and eight weeks of local therapy. A disease activity index, chosen as the major end point, decreased significantly after all three modes of treatment with no difference among groups. The endoscopic appearance of the mucosa and the histologic degree of inflammation was not different among groups. After eight weeks, fewer colonic segments were affected endoscopically following butyrate than placebo treatment. This study showed trends towards a beneficial effect of topical short-chain fatty acids in active ulcerative colitis, but more patients are needed to demonstrate this effect with sufficient statistical power.

<4>

Unique Identifier  
96186649

Authors

Patz J. Jacobsohn WZ. Gottschalk-Sabag S. Zeides S.  
Braverman DZ.

Institution

Department of Gastroenterology and Pathology, Shaare Zedek  
Medical Center, Jerusalem, Israel.

Title

Treatment of refractory distal ulcerative colitis with  
short chain fatty acid enemas.

Source

American Journal of Gastroenterology. 91(4):731-4. 1996  
Apr.

Abstract

OBJECTIVES: To determine the efficacy and safety of short chain fatty acids (SCFA) in the treatment of refractory distal ulcerative colitis (UC). METHODS: Ten patients with distal UC who had failed to respond to rectal and oral therapy with 5-ASA and corticosteroids were treated with twice daily enemas containing sodium acetate 60 mM, sodium propionate 30 mM, and sodium butyrate 40 mM titrated to a pH of 7. Patients were assessed clinically (rectal bleeding, tenesmus, bowel motions), endoscopically, and

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histologically before and after 6 wk of therapy. In addition, patients gave a self-assessment of the efficacy of treatment. RESULTS: Five of the 10 patients responded clinically, and four of these had a clinical remission as reflected by a decrease in degree of bleeding (2.2 vs. 1.2,  $p < 0.05$ ) and tenesmus (1.6 vs. 0.3,  $p < 0.05$ ) and by global self-assessment. Endoscopic improvement occurred in five (6.78 +/- 0.83 vs. 4.44 +/- 2.7,  $p < 0.05$ ). Histologically, no improvement was noted. No side effects were noted, and no patient's condition deteriorated. CONCLUSIONS: In this open-labeled study in patients with highly refractory distal UC, 50% had an overall clinical

assessed the treatment to be superior to previous treatments and expressed a desire to continue. This trial confirms other studies as to the efficacy of this treatment and further confirms the need for controlled trials of this promising therapy.

<5>

Unique Identifier  
96384844

Authors

al-Sabbagh R. Sinicrope FA. Sellin JH. Shen Y. Rouben L.

Institution

Division of Gastroenterology, University of Texas Medical School, Houston, USA.

Title

Evaluation of short-chain fatty acid enemas: treatment of radiation proctitis.

Source

American Journal of Gastroenterology. 91(9):1814-6. 1996 Sep.

Abstract

BACKGROUND: Radiation proctitis is a common complication of abdominal and pelvic radiotherapy; unfortunately, there is no established effective therapy for radiation proctitis. Short-chain fatty acids (SCFA) have been effectively used to treat a variety of colitides. We sought to determine whether SCFA enemas have a role in the treatment of radiation proctitis. METHODS: Seven patients completed an open-labeled, pilot study to evaluate the effect of SCFA on clinical, endoscopic, and pathological parameters of radiation proctitis. RESULTS: Four weeks of treatment with SCFA enemas resulted in clinical improvement in all patients. There were modest, but not significant, changes in endoscopic and pathological parameters. CONCLUSION: SCFA

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are a promising therapeutic option in radiation proctitis.

<6>

Unique Identifier  
93010164

Authors

Senagore AJ. MacKeigan JM. Scheider M. Ebrom JS.

Institution

Department of Surgical Research, Ferguson Clinic, Grand Rapids, Michigan.

Title

Short-chain fatty acid enemas: a cost-effective alternative in the treatment of nonspecific proctosigmoiditis [see comments].

Comments

Comment in: Dis Colon Rectum 1993 May;36(5):518

Source

Diseases of the Colon & Rectum. 35(10):923-7. 1992 Oct.

Abstract

The purpose of this study was to perform a randomized, prospective comparison of corticosteroid enemas (CS--100 mg

of hydrocortisone/60 cc P.R. q.h.s.; n = 12), mesalamine enemas (5-ASA--4 g/60 cc P.R. q.h.s.; n = 19), and short-chain fatty acid enemas (SCFA--60 cc P.R. b.i.d.; n = 14) for the treatment of proctosigmoiditis. Patients presenting to the Ferguson Clinic with the diagnosis of idiopathic proctosigmoiditis were evaluated for age, sex, prior history of proctitis, duration of symptoms prior to presentation, endoscopic scoring, and mucosal biopsies. Clinical evaluation was performed at two-week intervals for six weeks, with repeat biopsies taken at six weeks. There was no significant difference with respect to age, male/female ratio, past history of proctosigmoiditis, length of colorectum involved at the time of initial presentation, symptom resolution, and endoscopic and histologic improvement among the three treatment groups. Recovery occurred in a similar proportion in each of the three groups: CS, 10/12; 5-ASA, 17/19; and SCFA, 12/14. The cost of six weeks of treatment was: CS, \$71.82; 5-ASA, \$347.28; and SCFA, \$31.50. This study indicates that SCFA enemas are equally efficacious to CS or 5-ASA enemas for the treatment of proctosigmoiditis at a significant cost savings.

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Unique Identifier  
92266017

Page Number : 5

Authors

Silk DB.

Title

Medical management of severe inflammatory disease of the rectum: nutritional aspects. [Review] [101 refs]

Source

Baillieres Clinical Gastroenterology. 6(1):27-41, 1992 Mar.

Abstract

It is clear that the nutritional state of patients with inflammatory bowel disease is often impaired and can be improved by the provision of nutritional support. Improvement in nutritional status can be achieved as effectively with enteral as with parenteral nutrition. Nutritional support appears to have no primary therapeutic effect in patients with ulcerative colitis. With regard to nutritional support in Crohn's disease, parenteral nutrition should be restricted to use as supportive rather than primary therapy. Available information now seems to suggest that most of the benefits of parenteral nutrition in Crohn's disease are related to an improvement in nutritional state rather than as primary therapy, and its use should be restricted to the treatment of specific complications of Crohn's disease, such as intestinal obstruction related to stricture formation or short bowel syndrome following repeated resection. Although some doubt exists over the efficacy of oligopeptide-containing elemental and polymeric enteral diets, the present evidence indicates that chemically defined free amino acid-containing elemental diets have primary therapeutic efficacy in the management of acute exacerbations of

Crohn's disease. As such, these diets are worthy of therapeutic trial in patients with severe Crohn's disease involving the distal colon and rectum, particularly in those patients who are malnourished and who prove to be resistant to treatment with a combination of topical corticosteroids and 5-aminosalicylic acid-containing compounds. Clinicians should be aware, though, that the beneficial effects are likely to be restricted to the short term, with high relapse rates by 1 year, this being particularly so in patients with distal Crohn's proctocolitis (Teahon et al. 1988). Volatile fatty acid enemas clearly have potential in the management of patients with severe steroid-resistant proctitis. Finally, one of the most important observations made in recent years is the one concerning the large losses of nitrogen that will occur in patients with inflammatory bowel disease treated with corticosteroids in the absence of adequate protein intake (O'Keefe et al. 1989). Hopefully the days of treating

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patients with severe inflammatory bowel disease with high dose corticosteroids and a peripheral dextrose or dextrose-saline drip have passed into history. [References: 101]

<8>

Unique Identifier

93195263

Authors

Haque S. West AB.

Title

Diversion colitis--20 years a-growing [editorial].

Source

Journal of Clinical Gastroenterology. 15(4):281-3. 1992

Dec.

Abstract

During the last decade, clinical and pathologic studies of diversion colitis have led to a better understanding of its nature. The clinical features are well described, and the endoscopic appearances, and gross and microscopic pathology are now defined. Thus, firm diagnosis and distinction from other colitides, notably ulcerative colitis and Crohn's disease, are possible in most cases. Restoration of the fecal stream cures diversion colitis, which in some cases may be successfully treated with short-chain fatty acid enemas, although the efficacy of this method remains to be substantiated. An understanding of the pathogenesis of diversion colitis (currently unknown) may lead to better methods of prevention and treatment.



## **SODIUM BUTYRATE**

Has been reported to be irritating to eyes, skin and lungs. While its toxicological properties have not been thoroughly investigated, large doses have produced CNS depression in the rabbit. It has impaired cardiac function and decreased blood pressure in animals.

It has been used in enemas to treat colitis.



## REFERENCES

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4. Patz J, Jacobsohn WZ, Gottschalk-Sabag S, et al. Treatment of refractory distal ulcerative colitis with short chain fatty acid enemas. *American Journal of Gastroenterology* 1996; 91(4):731-4.
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